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## Co-Emergence of Specialized Endothelial Cells from Embryonic Stem Cells.

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### Public Summary:

A well-formed and robust vasculature is critical to the health of most organ systems in the body. However, the endothelial cells (ECs) forming the vasculature can exhibit a number of distinct functional subphenotypes like arterial or venous ECs, as well as angiogenic tip and stalk ECs. In this study, we investigate the in vitro differentiation of EC subphenotypes from embryonic stem cells (ESCs). Using our staged induction methods and chemically defined mediums, highly angiogenic EC subpopulations, as well as less proliferative and less migratory EC subpopulations, are derived. Furthermore, the EC subphenotypes exhibit distinct surface markers, gene expression profiles, and positional affinities during sprouting. While both subpopulations contained greater than 80% VE-cad(+)/CD31(+) cells, the tip/stalk-like EC contained predominantly Flt4(+)/Dll4(+)/CXCR4(+)/Flt-1(-) cells, while the phalanx-like EC was composed of higher numbers of Flt-1(+) cells. These studies suggest that the tip-specific EC can be derived in vitro from stem cells as a distinct and relatively stable EC subphenotype without the benefit of its morphological positioning in the sprouting vessel.

### Scientific Abstract:

A well-formed and robust vasculature is critical to the health of most organ systems in the body. However, the endothelial cells (ECs) forming the vasculature can exhibit a number of distinct functional subphenotypes like arterial or venous ECs, as well as angiogenic tip and stalk ECs. In this study, we investigate the in vitro differentiation of EC subphenotypes from embryonic stem cells (ESCs). Using our staged induction methods and chemically defined mediums, highly angiogenic EC subpopulations, as well as less proliferative and less migratory EC subpopulations, are derived. Furthermore, the EC subphenotypes exhibit distinct surface markers, gene expression profiles, and positional affinities during sprouting. While both subpopulations contained greater than 80% VE-cad(+)/CD31(+) cells, the tip/stalk-like EC contained predominantly Flt4(+)/Dll4(+)/CXCR4(+)/Flt-1(-) cells, while the phalanx-like EC was composed of higher numbers of Flt-1(+) cells. These studies suggest that the tip-specific EC can be derived in vitro from stem cells as a distinct and relatively stable EC subphenotype without the benefit of its morphological positioning in the sprouting vessel.

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